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10/018,878	03/06/2002	David Marin Anderson	PX3813USW	8728

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EXAMINER	
RAMIREZ, DELIA M	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,878	ANDERSON ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-48 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-48 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 06 March 2002 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-48 are pending.

Applicant's preliminary amendment of claims 5, 21, 31-32, 45, 47-48 in Paper No. 4, filed on 12/19/2001, is acknowledged.

Specification

1. The use of the trademarks has been noted in pages 14-28 of this application. See, for example, "Sigma", Stratagene", etc. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Priority

2. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/141,827 filed on 07/01/1999.

3. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. 119(a)-(d) to PCT/GB00/02357 filed on 06/30/2000.

4. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 09/345,492 filed on 07/01/1999.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 12/19/2001 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

6. The drawings have been reviewed and are objected under 37 CFR 1.84 or 1.152. See attached Notice of Draftsperson's Patent Drawing Review. Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDOMENT of the application. In addition, if amendments to the specification are needed due to drawing corrections, Applicant is requested to submit such amendments while the case is being prosecuted to expedite the processing of the application.

Claim Objections

7. Claim 5 is objected to because of the following informalities: the term "extrachromosomal vector" is redundant because the commonly accepted meaning of the term "vector" is that of DNA, which is not part of the chromosome, used to "carry" foreign DNA (Lewin, Genes IV, page 807, 1990). It is suggested that the word "extrachromosomal" be deleted. Appropriate correction is required.

8. Claim 22 is objected to because of the following informalities: for clarity, it is suggested that the term "the" be inserted before the term "td". Appropriate correction is required.

9. Claim 25 is objected to because of the recitation of "(in terms of reading frame)". The term "downstream" within the context of the claim is understood as written, therefore the term in parentheses is unnecessary. However if applicants wish to emphasize what the meaning of the term is within the context of the claim, it is suggested that the parentheses be deleted and the term be incorporated accordingly. Appropriate correction is required.

10. Claim 33 is objected to because of the following informalities: for clarity, it is suggested that the term "according to any of the preceding claims" be replaced with "according to any one of claims 1-32". Appropriate correction is required.

11. Claim 35 is objected to because of the following informalities: for clarity, it is suggested that a comma be inserted between the terms "low levels of" and "or no uracil DNA glycosylase activity". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claim 1 (claims 2-48 dependent thereon) is indefinite in the recitation of "unit which comprises a ribonucleotide reductase gene and a thioredoxin gene or a uridine kinase gene and/or a dCTP deaminase gene" for the following reasons. As written, there are at least two interpretations of what the transcriptional unit can comprise. In one interpretation, the unit can

comprise either (a) a ribonucleotide reductase gene and a thioredoxin gene, (b) a uridine kinase gene, (c) a dCTP deaminase gene, or (d) a uridine kinase gene and a dCTP deaminase gene. In another interpretation, the unit can comprise either (a) a ribonucleotide reductase gene and a thioredoxin gene, (b) a ribonucleotide reductase gene and a uridine kinase gene, (c) a ribonucleotide reductase gene and a dCTP deaminase gene, (d) a ribonucleotide reductase gene, a thioredoxin gene and a dCTP deaminase gene, or (e) a ribonucleotide reductase gene, a uridine kinase gene and a dCTP deaminase gene. It is suggested that the claim be amended to itemize each of the combination of genes which can be part of the transcriptional unit. For examination purposes, the first interpretation provided above will be used. Correction is required.

15. Claims 7-10, 15-18, 22-28, 31-32 (claims 19-20, 33-48 dependent thereon) are indefinite in the recitation of "nrdA, nrdB, nrdC, td, udk, dcd, ung" for the following reasons. While the gene nomenclature used may be appropriate for E. coli or T phage genes, the use of this nomenclature for genes encoding proteins of identical function in other organisms may not be accurate. As known in the art, genes encoding proteins of identical function in two different organisms may use different designations. For example, the ARO4 gene of Candida albicans encodes a DAHP synthase whereas the E. coli counterpart is the aroF gene. See the abstract of Sousa et al. (Microbiology 148(Pt5):1291-1303), attached to this Office Action. It is also noted that the E. coli counterpart of the td gene is the thyA gene and the E. coli counterpart of the nrdC gene in T4 is the trxA gene. As such, the use of gene terminology which is applicable to some organisms and not to others is confusing since the claims use this gene nomenclature with respect to any organism. For examination purposes, the terms "nrdA, nrdB, nrdC, td, udk, dcd, ung" will be interpreted as "gene encoding ribonucleotide reductase A, ribonucleotide reductase

B, thioredoxin, thymidylate synthase, uridine kinase, dCTP deaminase, uracil DNA glycosylase". If Applicants wish to use the recited terminology in the claims, it is suggested that the claims be amended to clearly indicate the organism associated with the specific gene designation. Correction is required.

16. Claim 14 is indefinite in the recitation of "synthetic terminator" as it is unclear what the meaning of the term is. It is suggested that if applicants intended termination sequence refers to one from a different gene, the term "heterologous termination sequence" or "recombinant termination sequence" be used.

17. Claim 15 (claims 16-17 dependent thereon) is indefinite in the recitation of "reductase encoded by the unit is less sensitive to allosteric inhibition than the ribonucleotide reductase encoded by the unit comprising an unmodified nrdA gene" because it is unclear which ribonucleotide reductases are being compared with the term "less sensitive to". As written, one can not ascertain if the modified and unmodified ribonucleotide reductases being compared are the modified reductase and its wild-type counterpart or if the modified reductase and the unmodified reductase are not related at all. The term "less sensitive to", which is a relative term, is indefinite because the basis for comparison cannot be determined from the claim or the specification. It is suggested that if the comparison is being made between two versions of the same enzyme, the claim be amended to recite more clear and unambiguous language such as "reductase encoded by the unit is less sensitive to allosteric inhibition than the wild-type equivalent of said reductase" or similar. For examination purposes, the comparison recited in the claim will be interpreted as being between a modified reductase and the wild-type equivalent of said reductase. Correction is required.

18. Claims 17 and 42 are indefinite in the recitation of "position 79 in the nrdA expression product" because it is unclear which position is being referred without indicating the specific sequence to which position 79 is associated to. Since the claim reads on any nrdA expression product (from any species), there is no specific sequence associated with position 79. It is suggested that applicants amend the claim to include a numerical sequence identifier (SEQ ID NO: #) if the sequence has been disclosed in the sequence listing or to clearly identify the sequence to which position 79 is associated to in the claim. Correction is required.

19. Claim 23 is indefinite in the recitation of "construct according to claim 22 wherein td gene is located in the same vector as the nrdA, nrdB and nrdC genes" for the following reasons. As written, the claim implies that the td gene can also be located in a different vector from that containing the nrdA, nrdB and nrdC genes. However, it is unclear how the td gene and the nrdA, nrdB and nrdC genes can be in different vectors if they are all part of the same DNA construct. As such, claim 23 is not further limiting claim 22. For examination purposes, the limitation recited in claim 23 will not be given patentable weight. Correction is required.

20. Claim 35 (claim 36 dependent thereon) is indefinite in the recitation of "one or more host cell DNA sequences encoding for uracil DNA glycosylase activity have been modified" as it is unclear how a sequence encodes activity. As known in the art, a sequence is a graphical representation of the order in which nucleotides are arranged in a polynucleotide. Therefore, a sequence cannot encode activity. It is suggested that the term "sequences" be replaced with "polynucleotides". For examination purposes, the interpretation above will be used. Correction is required.

21. Claim 36 is indefinite in the recitation of "wherein the host cell DNA sequence is an ung gene" as it is unclear how a sequence can be a gene. As known in the art and indicated above, a sequence is a graphical representation of the order in which nucleotides are arranged in a polynucleotide or in a gene. It is suggested that the term "sequence" be replaced with "polynucleotide". For examination purposes, the interpretation above will be used. Correction is required.

22. Claim 37 is indefinite in the recitation of "host cell DNA sequences ...have been removed" as it is unclear how one can remove sequences from a cell. See meaning of the term "sequence" discussed above. It is suggested that the term "sequences" be replaced with "polynucleotides". For examination purposes, the interpretation above will be used. Correction is required.

23. Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The instant claim is drawn to a process for making azidothymidine comprising culturing a host cell according to claim 33. However culturing a host cell according to claim 33 will not produce azidothymidine but rather thymidine, which is a precursor. It is suggested that the claim be amended to include a step indicating the conversion of thymidine to azidothymidine. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

24. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

25. Claims 1-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-33 are directed to genera of constructs comprising genes from any organism encoding genera of ribonucleotide reductases, thioredoxins, thymidylate synthases, uridine kinases, and/or dCTP deaminases. See claim rejections under 35 USC 112, second paragraph for description of gene combinations as interpreted. Claim 33 is drawn to a genus of host cells comprising the genera of constructs described above. Claims 45-47 are directed to a method of producing deoxyribonucleosides with the genus of cells of claim 33. Claim 48 is directed to a culture medium comprising the genus of cells of claim 33. Claims 34-38 are drawn to a genus of modified host cells comprising the constructs as described above wherein the modification results in low or no uracil DNA glycosylase activity. Claim 39 is directed to the host cell of claim 38 as described above with the added limitation that the host cell is either E. coli, Salmonella, Pseudomonas, Bacillus or Saccharomyces. Claims 40-44 are directed to a genus of modified organisms wherein the modification results in repressed or no uracil DNA glycosylase activity and wherein the genus of organisms further comprises genera of DNA constructs comprising genes from any organism encoding genera of ribonucleotide reductases, thioredoxins, thymidylate synthases, uridine kinases, and/or dCTP deaminases.

The specification discloses the construction of a DNA construct comprising the T4 phage genes encoding ribonucleotide reductase A, B, and thioredoxin (nrdA, nrdB, and nrdC; Example

1), a DNA construct comprising T4 nrdA, nrdB, nrdC and the T4 gene encoding thymidylate synthase (Example 3), and constructs further comprising the E. coli dcd and/or the udk genes (Examples 7 and 8). The specification also teaches the construction of a T4 nrdA mutant wherein the mutation results in an Ala to Ile amino acid substitution at position 79 in the T4 ribonucleotide reductase A product. In addition, the specification discloses the construction of an E. coli strain wherein the ung gene has been disrupted so that no uracil DNA glycosylase is produced. While the specification discloses the constructs and strains as discussed above, there is no description of other genes encoding the enzymes as encompassed by the claims from other organisms. In addition, there is no disclosure which amino acid substitutions in other ribonucleotide reductases from other organisms can be made which would result in less sensitivity to allosteric inhibition. Furthermore, there is no disclosure of the structure of other genes in other organisms which encode uracil DNA glycosylase activity or the modifications which would result in repressed or no uracil DNA glycosylase activity, with the exception of an inactivating insertion in the ung gene of an E. coli cell.

While one could argue that the constructs, host cells, medium and processes claimed are adequately described since one can isolate additional polynucleotides from other organisms encoding the enzymes recited in the claims by sequence comparison with structures known in the art or those disclosed in the instant application, the state of the art teaches that sequence comparison alone should not be used to determine a protein's function and that small amino acid changes can drastically change the function of a polypeptide. Bork (Genome Research, 10:398-400, 2000) teaches protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995)

teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* where found to be hydroxylases once tested for activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. The specification only discloses a few species of the genera of constructs, which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the genera of constructs, host cells, media and methods claimed. Thus, one skilled in the art cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

26. Claims 1-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) DNA constructs comprising the T4 phage nrdA, nrdB, nrdC, and td genes, (2) DNA constructs further comprising the E. coli udk and/or dcd genes, (3) an E. coli host cell wherein the uracil DNA glycosylase is absent due to an inactivating insertion in the ung gene, and (4) a T4 nrdA mutant which encodes a ribonucleotide reductase A which is less sensitive to allosteric inhibition when compared to the wild-type counterpart, does not reasonably provide enablement for (1) DNA constructs wherein the polynucleotides encoding the enzymes of the DNA constructs are isolated from any organism, (2) any host cell modified in any way so that it no longer displays uracil DNA glycosylase activity, (3) any ribonucleotide

reductase modified to display less allosteric inhibition than its wild-type counterpart. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims as described above is not commensurate with the enablement provided in regard to the extremely large number of unknown genes required to make the DNA constructs, the large number of unknown polynucleotides from other organisms which encode uracil DNA glycosylases, and the large number of unknown ribonucleotide reductases from any organism which display less allosteric inhibition than their wild-type counterparts. As indicated above, the state of the art teaches the unpredictability of isolating polynucleotides encoding proteins of similar function based on sequence homology. See the teachings of Bork (Genome Research, 10:398-400, 2000), Broun et al. (Science 282:1315-1317, 1998), Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) and Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) already discussed. In addition, since the amino acid sequence in a protein determines its function, one of skill in the art would require some knowledge or guidance as to how structure relates to function to make ribonucleotide reductases which are less sensitive to allosteric inhibition compared to the wild-type counterpart. Therefore, due to the lack of relevant

examples, the amount of information provided, the lack of knowledge about the critical structural elements which relate to function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to (1) screen and isolate those polynucleotides, as encompassed by the claim, which encode enzymes of similar function as those recited in the claims, and (2) determine which modifications in the structure of a ribonucleotide reductase will result in less allosteric inhibition. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

27. Claims 1, 3, 5-6, 11, 12, 32, 33, 45-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. (J. Bacteriol. 174(17):5647-5653, 1992). Wang et al. teaches cloning and expression of E. coli dCTP deaminase (dcd gene). Wang et al. teaches vectors and host cells comprising the dcd gene as well as production of the dCTP deaminase by culturing host cells comprising the vectors (page 5647, column 1, Bacterial strains and plasmids; page 5648, column 2, Induction of dcd in expression vectors).

Claims 1, 3, 5-6, 11-12, 14, 32 are directed to a DNA construct comprising a gene encoding dCTP deaminase, a DNA construct further comprising regulatory elements, vectors comprising the construct, and host cells transformed with vectors comprising the construct (modified cells). Since the expression vector of Wang et al. (pET-11, T7 promoter; page 5647,

second column, lines 3-5) is a DNA construct which comprises the dcd gene and it is used for production of the corresponding protein, it has regulatory elements such as promoter, operator, termination sequence, initiation sequence and ribosome binding site. In addition, the pET-11 plasmid has a T7 termination sequence (i.e. heterologous; see claim interpretation in claim rejections under 35 USC 112, second paragraph). As such, the teachings of Wang et al. anticipates the instant claims as written. Claims 45-46 are directed to a method which comprises culturing a host cell containing a vector which comprises the DNA construct. Since Wang et al. teaches the culturing of a host cell which is transformed with a vector comprising the construct, the teachings of Wang et al. also anticipate claims 45-46 as written.

Claim Rejections - 35 USC § 103

28. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

29. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

30. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (J. Bacteriol. 174(17):5647-5653, 1992) in view of Lim et al. (Biotechnol. Prog. 14:548-553, 1998). The teachings of Wang et al. have been discussed above. Wang et al. does not teach a DNA construct wherein the promoter is the lambda P_L promoter. Lim et al. teaches an expression vector containing the IFN-γ gene wherein the promoter is a lambda P_L promoter (page 548, second column, Materials and Methods). Lim et al. does not teach a DNA construct comprising a polynucleotide encoding dCTP deaminase.

Claim 13 is directed to the construct of claim 12 as described above with the added limitation that the promoter is the lambda P_L promoter.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an expression vector, as taught by Wang et al., wherein the promoter is a lambda P_L promoter, as taught by Lim et al. A person of ordinary skill in the art is motivated to construct such a vector since induction of protein expression with a lambda P_L promoter only requires a temperature shift, which is advantageous since no additional expensive chemicals, such as IPTG, are required for protein expression. One of ordinary skill in the art has a reasonable expectation of success at making a DNA construct which uses a lambda P_L promoter since Lim et al. use such a construct with a different protein. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Double Patenting

31. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

32. Claims 1-44, 48 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12, 14-17, 29-38, 44-46, 50-61 of copending Application No. 09/345492. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 12, 14-17, 29-38, 44-46, 50-61 of copending Application No. 09/345492 are directed to a DNA construct comprising polynucleotides encoding T4 nrdA or T4 nrdB expression products, and further comprising the T4 nrdC expression product, wherein the T4 nrdA (ribonucleotide reductase A) expression product is modified such that it is less sensitive to allosteric inhibition than the wild-type counterpart, host cells comprising said construct, and media used to culture said host cells. Claims 1-44, 48 of the instant application are drawn in part to a DNA construct

comprising genes from any organism encoding genera of ribonucleotide reductases and thioredoxins, host cells comprising such constructs, and media used to culture such cells. Therefore, claims 12, 14-17, 29-38, 44-46, 50-61 of copending Application No. 09/345492 anticipate claims 1-44, 48 of the instant application as written.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

33. No claim is in condition for allowance.

34. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

35. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
March 9, 2003

REBECCA E. PRUTY
PRIMARY EXAMINER
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